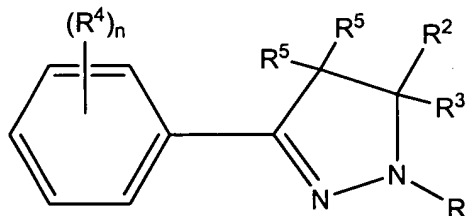


Amendments to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the application:

Listing of Claims

1. (Currently amended) A method of modulating an endothelial gene differentiation-1
("Edg-1") Edg-1 receptor mediated biological activity for vasoconstriction, comprising
contacting a cell expressing the Edg-1 receptor with an amount of a non-phospholipid
modulator of the Edg-1 receptor sufficient to modulate the Edg-1 receptor mediated
biological activity for vasoconstriction, wherein the modulator is not a phospholipid;
wherein said modulator is a compound of Formula (Ia):



(Ia)

or a pharmaceutically acceptable solvate or hydrate thereof, wherein

n is a member selected from the integers 0 to 5;

R^1 is a member selected from the group consisting of hydrogen, alkyl, substituted alkyl,

acyl, substituted acyl, acylamino, substituted acylamino, alkylamino, substituted

alkylamino, alkylthio, substituted alkylthio, alkoxy, substituted alkoxy,

alkoxycarbonyl, substituted alkoxycarbonyl, alkylarylamino, substituted

alkylarylamino, arylalkyloxy, substituted arylalkyloxy, amino, aryl, substituted

aryl, arylalkyl, substituted arylalkyl, arylamino, substituted arylamino,

arylsulfonyl, substituted arylsulfonyl, carboxy, carbamoyl, substituted carbamoyl,

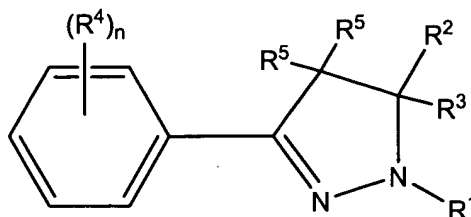
cycloalkyl, substituted cycloalkyl, cycloheteroalkyl, substituted cycloheteroalkyl,

dialkylamino, substituted dialkylamino, heteroaryloxy, substituted heteroaryloxy,

heteroaryl, substituted heteroaryl, heteroalkyl, and substituted heteroalkyl;

each R^2 , R^3 and R^5 is a member independently selected from the group consisting of
hydrogen, alkyl, substituted alkyl, acyl, substituted acyl, acylamino, substituted
acylamino, alkylamino, substituted alkylamino, alkylthio, substituted alkylthio,
alkoxy, substituted alkoxy, alkoxycarbonyl, substituted alkoxycarbonyl,
alkylarylamino, substituted alkylarylamino, arylalkyloxy, substituted
arylalkyloxy, amino, aryl, substituted aryl, arylalkyl, substituted arylalkyl,
arylamino, substituted arylamino, arylsulfonyl, substituted arylsulfonyl, carboxy,
carbamoyl, substituted carbamoyl, cycloalkyl, substituted cycloalkyl,
cycloheteroalkyl, substituted cycloheteroalkyl, dialkylamino, substituted
dialkylamino, heteroaryloxy, substituted heteroaryloxy, heteroaryl, substituted
heteroaryl, heteroalkyl, substituted heteroalkyl, hydroxyl, nitro and thio; and
each R^4 is a member independently selected from the group consisting of hydrogen, halo,
alkyl, substituted alkyl, acyl, substituted acyl, acylamino, substituted acylamino,
alkylamino, substituted alkylamino, alkylthio, substituted alkylthio, alkoxy,
substituted alkoxy, alkoxycarbonyl, substituted alkoxycarbonyl, alkylarylamino,
substituted alkylarylamino, arylalkyloxy, substituted arylalkyloxy, amino, aryl,
substituted aryl, arylalkyl, substituted arylalkyl, arylsulfonyl, substituted
arylsulfonyl, azido, carboxy, carbamoyl, substituted carbamoyl, carboxyl, cyano,
cycloalkyl, substituted cycloalkyl, cycloheteroalkyl, substituted cycloheteroalkyl,
dialkylamino, substituted dialkylamino, halo, heteroaryloxy, substituted
heteroaryloxy, heteroaryl, substituted heteroaryl, heteroalkyl, substituted
heteroalkyl, hydroxyl, nitro and thio.

2. (Currently amended) A method of modulating an Edg-1 receptor mediated biological
activity for vasoconstriction in a subject, comprising administering to the subject a
therapeutically effective amount of a non-phospholipid modulator of the Edg-1 receptor,
~~wherein the modulator is not a phospholipid.~~ wherein said modulator is a compound of
Formula (Ia):



(Ia)

or a pharmaceutically acceptable solvate or hydrate thereof, wherein:

n is a member selected from the integers 0 to 5;

R^1 is a member selected from the group consisting of hydrogen, alkyl, substituted alkyl,

acyl, substituted acyl, acylamino, substituted acylamino, alkylamino, substituted

alkylamino, alkylthio, substituted alkylthio, alkoxy, substituted alkoxy,

alkoxycarbonyl, substituted alkoxycarbonyl, alkylarylamino, substituted

alkylarylamino, arylalkyloxy, substituted arylalkyloxy, amino, aryl, substituted

aryl, arylalkyl, substituted arylalkyl, arylamino, substituted arylamino,

arylsulfonyl, substituted arylsulfonyl, carboxy, carbamoyl, substituted carbamoyl,

cycloalkyl, substituted cycloalkyl, cycloheteroalkyl, substituted cycloheteroalkyl,

dialkylamino, substituted dialkylamino, heteroaryloxy, substituted heteroaryloxy,

heteroaryl, substituted heteroaryl, heteroalkyl, and substituted heteroalkyl;

each R^2 , R^3 and R^5 is a member independently selected from the group consisting of

hydrogen, alkyl, substituted alkyl, acyl, substituted acyl, acylamino, substituted

acylamino, alkylamino, substituted alkylamino, alkylthio, substituted alkylthio,

alkoxy, substituted alkoxy, alkoxycarbonyl, substituted alkoxycarbonyl,

alkylarylamino, substituted alkylarylamino, arylalkyloxy, substituted

arylalkyloxy, amino, aryl, substituted aryl, arylalkyl, substituted arylalkyl,

arylamino, substituted arylamino, arylsulfonyl, substituted arylsulfonyl, carboxy,

carbamoyl, substituted carbamoyl, cycloalkyl, substituted cycloalkyl,

cycloheteroalkyl, substituted cycloheteroalkyl, dialkylamino, substituted

dialkylamino, heteroaryloxy, substituted heteroaryloxy, heteroaryl, substituted

heteroaryl, heteroalkyl, substituted heteroalkyl, hydroxyl, nitro and thio; and

each R⁴ is a member independently selected from the group consisting of hydrogen, halo, alkyl, substituted alkyl, acyl, substituted acyl, acylamino, substituted acylamino, alkylamino, substituted alkylamino, alkylthio, substituted alkylthio, alkoxy, substituted alkoxy, alkoxycarbonyl, substituted alkoxycarbonyl, alkylarylamino, substituted alkylarylamino, arylalkyloxy, substituted arylalkyloxy, amino, aryl, substituted aryl, arylalkyl, substituted arylalkyl, arylsulfonyl, substituted arylsulfonyl, azido, carboxy, carbamoyl, substituted carbamoyl, carboxyl, cyano, cycloalkyl, substituted cycloalkyl, cycloheteroalkyl, substituted cycloheteroalkyl, dialkylamino, substituted dialkylamino, halo, heteroaryloxy, substituted heteroaryloxy, heteroaryl, substituted heteroaryl, heteroalkyl, substituted heteroalkyl, hydroxyl, nitro and thio.

3. (Canceled)

4. (Original) The method of Claim 1 or 2, wherein the modulator is an antagonist.

5. (Currently amended) The method of Claim 1 or 2, wherein the modulator exhibits at least about 200 fold inhibitory selectivity for Edg-1 relative to ~~other Edg~~ Edg-2, Edg-4 and Edg-7 receptors.

6. (Currently amended) The method of Claim 1 or 2, wherein the modulator exhibits at least about 100 fold inhibitory selectivity for Edg-1 relative to ~~other Edg~~ Edg-2, Edg-4 and Edg-7 receptors.

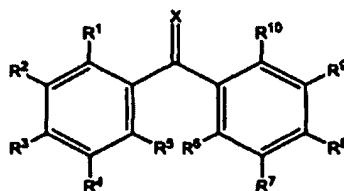
7. (Currently amended) The method of Claim 1 or 2, wherein the modulator exhibits at least about 20 fold inhibitory selectivity for Edg-1 relative to ~~other Edg~~ Edg-2, Edg-4 and Edg-7 receptors.

8. (Currently amended) The method of Claim 1 or 2, wherein the ~~inhibitor~~ modulator exhibits at least about 5 fold inhibitory selectivity for Edg-1 relative to ~~other Edg~~ Edg-2, Edg-4 and Edg-7 receptors.

- 1 9. (Currently amended) The method of Claim 1 or 2, wherein the ~~inhibitor~~ modulator
2 exhibits at least about 200 fold inhibitory selectivity for Edg-1 relative to Edg-3, Edg-5,
3 Edg-6 and Edg-8 receptors.
- 1 10. (Currently amended) The method of Claim 1 or 2, wherein the ~~inhibitor~~ modulator
2 exhibits at least about 100 fold inhibitory selectivity for Edg-1 relative to Edg-3, Edg-5,
3 Edg-6 and Edg-8 receptors.
- 1 11. (Currently amended) The method of Claim 1 or 2, wherein the ~~inhibitor~~ modulator
2 exhibits at least about 20 fold inhibitory selectivity for Edg-1 relative to Edg 3, Edg-5,
3 Edg-6 and Edg-8 receptors.
- 1 12. (Currently amended) The method of Claim 1 or 2, wherein the ~~inhibitor~~ modulator
2 exhibits at least about 5 fold inhibitory selectivity for Edg-1 relative to Edg-3, Edg-5,
3 Edg-6 and Edg-8 receptors.
- 1 13. (Withdrawn) The method of Claim 1 or 2, wherein the biological activity is cell
2 proliferation.
- 1 14. (Canceled)
- 1 15. (Canceled)
- 1 16. (Canceled)
- 1 17. (Canceled)
- 1 18. (Withdrawn, Currently amended) The method of Claim 13, wherein cell proliferation
2 leads to cancer selected from the group consisting of ovarian cancer, peritoneal cancer,
3 endometrial cancer, cervical cancer, breast cancer, colon cancer ~~or~~ and prostate cancer.
- 1 19. (Withdrawn) The method of Claim 13, wherein cell proliferation is stimulated by S1P.

- 1 **20.** (Canceled)
- 1 **21.** (Currently amended) The method of Claim 1 or 2 wherein the modulator binds to the
2 Edg-1 receptor with a binding constant between about 1 femtomolar to about 10 μ M to
3 ~~about 1 fM~~.
- 1 **22.** (Original) The method of Claim 1 or 2 wherein the modulator binds to the Edg-1 receptor
2 with a binding constant of at least about 1 μ M.
- 1 **23.** (Original) The method of Claim 1 or 2 wherein the modulator binds to the Edg-1 receptor
2 with a binding constant of at least about 10 nM.
- 1 **24.** (Withdrawn) The method of Claim 1 or 2, wherein the modulator is a nucleic acid,
2 peptide or carbohydrate.
- 1 **25.** (Original) The method of Claim 1 or 2, wherein the modulator is an organic molecule of
2 molecular weight of less than 750 daltons.
- 1 **26.** (Withdrawn, Currently amended) The method of Claim 1, wherein the cell is a member
2 selected from the group consisting of a HTC hepatoma cell, an ovarian cell, an epithelial
3 cell, a fibroblast cell, a neuronal cell, a carcinoma cell, a pheochromocytoma cell, a
4 myoblast cell, a platelet cell ~~or~~ and a fibrosarcoma cell.
- 1 **27.** (Withdrawn, Currently amended) The method of Claim 21, wherein the cell is a member
2 selected from the group consisting of OV202 human ovarian cell, a HTC rat hepatoma
3 cell, a CAOV-3 human ovarian cancer cell, MDA-MB-453 breast cancer cell, MDA-MB-
4 231 breast cancer cell, HUVEC cells A431 human epitheloid carcinoma cell ~~or~~ and a HT-
5 1080 human fibrosarcoma cell.
- 1 **28.** (Canceled)

29. (Withdrawn, Currently amended) ~~The method of Claim 1 or 2,~~ A method of modulating an Edg-1 receptor mediated biological activity, comprising contacting a cell expressing the Edg-1 receptor with an amount of a non-phospholipid modulator of the Edg-1 receptor sufficient to modulate the Edg-1 receptor mediated biological activity, wherein the modulator is a compound of structural formula Formula (II):



(II)

or a pharmaceutically available acceptable solvate or hydrate thereof, wherein:

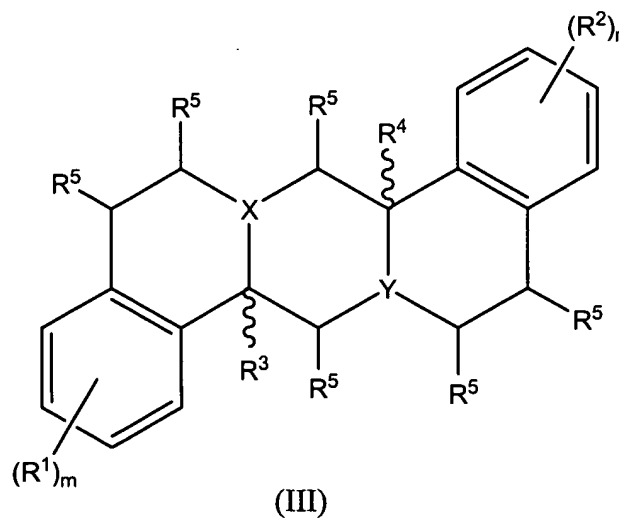
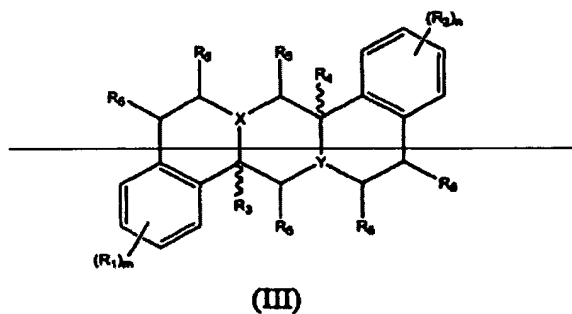
X is a member selected from the group consisting of O or and S;

each R¹, R², R³, R⁴ and R⁵ is a member independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, acyl, substituted acyl, acylamino, substituted acylamino, alkylamino, substituted alkylamino, alkylthio, substituted alkylthio, alkoxy, substituted alkoxy, alkoxycarbonyl, substituted alkoxycarbonyl, alkylaryl amino, substituted alkylaryl amino, arylalkyloxy, substituted arylalkyloxy, amino, aryl, substituted aryl, arylalkyl, substituted arylalkyl, arylsulfonyl, substituted arylsulfonyl, azido, carboxy, carbamoyl, substituted carbamoyl, carboxyl, cyano, cycloalkyl, substituted cycloalkyl, cycloheteroalkyl, substituted cycloheteroalkyl, dialkylamino, substituted dialkylamino, halo, heteroaryloxy, substituted heteroaryloxy, heteroaryl, substituted heteroaryl, heteroalkyl, substituted heteroalkyl, hydroxyl, nitro or and thio; and

each R⁶, R⁷, R⁸ and R¹⁰ is a member independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, acyl, substituted acyl, acylamino, substituted acylamino, alkylamino, substituted alkylamino, alkylthio, substituted alkylthio, alkoxy, substituted alkoxy, alkoxycarbonyl, substituted alkoxycarbonyl, alkylaryl amino, substituted alkylaryl amino,

26 arylalkyloxy, substituted arylalkyloxy, amino, aryl, substituted aryl, arylalkyl,
27 substituted arylalkyl, arylsulfonyl, substituted arylsulfonyl, azido, carboxy,
28 carbamoyl, substituted carbamoyl, carboxyl, cyano, cycloalkyl, substituted
29 cycloalkyl, cycloheteroalkyl, substituted cycloheteroalkyl, dialkylamino,
30 substituted dialkylamino, halo, heteroaryloxy, substituted heteroaryloxy,
31 heteroaryl, substituted heteroaryl, heteroalkyl, substituted heteroalkyl,
32 hydroxyl, nitro or and thio.

- 1 30. (Withdrawn, Currently amended) The method of Claim 1 or 2, A method of modulating
2 an Edg-1 receptor mediated biological activity, comprising contacting a cell expressing
3 the Edg-1 receptor with an amount of a non-phospholipid modulator of the Edg-1
4 receptor sufficient to modulate the Edg-1 receptor mediated biological activity, wherein
5 the modulator is a compound of structural formula Formula (III):



8 or a pharmaceutically ~~available~~ acceptable solvate or hydrate thereof, wherein:

9 n is a member selected from the integers 1 to 4 ~~1, 2, 3, 4 or 5~~;

10 m is a member selected from the integers 1 to 4 ~~1, 2, 3, 4, or 5~~;

11 each X and Y is a member independently selected from the group consisting of C or
12 and N; and

13 each R¹, R², R³, R⁴ and R⁵ is a member independently selected from the group
14 consisting of hydrogen, alkyl, substituted alkyl, acyl, substituted acyl,
15 acylamino, substituted acylamino, alkylamino, substituted alkylamino,
16 alkylthio, substituted alkylthio, alkoxy, substituted alkoxy, alkoxycarbonyl,
17 substituted alkoxycarbonyl, alkylaryl amino, substituted alkylaryl amino,
18 arylalkyloxy, substituted arylalkyloxy, amino, aryl, substituted aryl, arylalkyl,
19 substituted arylalkyl, arylsulfonyl, substituted arylsulfonyl, azido, carboxy,
20 carbamoyl, substituted carbamoyl, carboxyl, cyano, cycloalkyl, substituted
21 cycloalkyl, cycloheteroalkyl, substituted cycloheteroalkyl, dialkylamino,
22 substituted dialkylamino, halo, heteroaryloxy, substituted heteroaryloxy,
23 heteroaryl, substituted heteroaryl, heteroalkyl, substituted heteroalkyl,
24 hydroxyl, nitro ~~or~~ and thio.

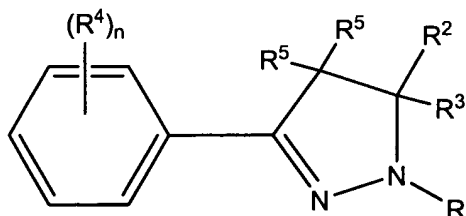
1 31. (Withdrawn, Currently amended) A method for treating ~~or preventing~~ a disease or
2 condition selected from the group consisting of cancers, acute lung diseases, acute
3 inflammatory exacerbation of chronic lung diseases, surface epithelial cell injury, ~~or and~~
4 cardiovascular diseases in a subject in need of such treatment, said method comprising
5 administering to a said subject ~~in need of such treatment or prevention~~ a therapeutically
6 effective amount of a compound of ~~structural formula~~ Formulae (I), (II) or (III).

1 32. (Withdrawn, Currently amended) A method for treating ~~or preventing~~ a disease or
2 condition selected from the group consisting of ovarian cancer, peritoneal cancer,
3 endometrial cancer, cervical cancer, breast cancer, colorectal cancer, uterine cancer,
4 stomach cancer, small intestine cancer, thyroid cancer, lung cancer, kidney cancer,
5 pancreas cancer, prostate cancer, adult respiratory distress syndrome (ARDS), asthma,

transcorneal freezing, cutaneous burns, ischemia ~~or~~ and atherosclerosis in a subject in need of such treatment, said method comprising administering to a said subject in need of such treatment or prevention a therapeutically effective amount of a compound of structural formula Formulae (I), (II) or (III).

33. (Canceled)

34. (Currently amended) A method for treating ~~or preventing~~ vasoconstriction in cerebral arteries, ~~systemic lupus erythematosus, rheumatoid arthritis, non-glomerular nephrosis, psoriasis, chronic active hepatitis, ulcerative colitis, Crohn's disease, Behcet's disease, chronic glomerulonephritis, chronic thrombocytopenic purpura, autoimmune hemolytic anemia, migraine headache, stroke, subarachnoid hemorrhage, or a vasospasm~~ in a subject in need of such treatment, said method comprising administering to a said subject in need of such treatment or prevention a therapeutically effective amount of a compound of structural formula Formula (Ia), (II) or (III), wherein said compound of Formula (Ia) is:



(Ia)

or a pharmaceutically acceptable solvate or hydrate thereof, wherein

n is a member selected from the integers 0 to 5;

R^1 is a member selected from the group consisting of hydrogen, alkyl, substituted

alkyl, acyl, substituted acyl, acylamino, substituted acylamino, alkylamino,

substituted alkylamino, alkylthio, substituted alkylthio, alkoxy, substituted

alkoxy, alkoxycarbonyl, substituted alkoxycarbonyl, alkylarylamino,

substituted alkylarylamino, arylalkyloxy, substituted arylalkyloxy, amino,

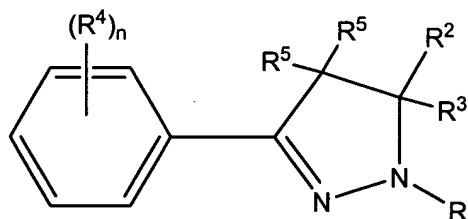
aryl, substituted aryl, arylalkyl, substituted arylalkyl, arylamino, substituted

arylamino, arylsulfonyl, substituted arylsulfonyl, carboxy, carbamoyl,
substituted carbamoyl, cycloalkyl, substituted cycloalkyl, cycloheteroalkyl,
substituted cycloheteroalkyl, dialkylamino, substituted dialkylamino,
heteroaryloxy, substituted heteroaryloxy, heteroaryl, substituted heteroaryl,
heteroalkyl, and substituted heteroalkyl;

each R², R³ and R⁵ is a member independently selected from the group consisting of
hydrogen, alkyl, substituted alkyl, acyl, substituted acyl, acylamino,
substituted acylamino, alkylamino, substituted alkylamino, alkylthio,
substituted alkylthio, alkoxy, substituted alkoxy, alkoxycarbonyl, substituted
alkoxycarbonyl, alkylarylamino, substituted alkylarylamino, arylalkyloxy,
substituted arylalkyloxy, amino, aryl, substituted aryl, arylalkyl, substituted
arylalkyl, arylamino, substituted arylamino, arylsulfonyl, substituted
arylsulfonyl, carboxy, carbamoyl, substituted carbamoyl, cycloalkyl,
substituted cycloalkyl, cycloheteroalkyl, substituted cycloheteroalkyl,
dialkylamino, substituted dialkylamino, heteroaryloxy, substituted
heteroaryloxy, heteroaryl, substituted heteroaryl, heteroalkyl, substituted
heteroalkyl, hydroxyl, nitro and thio; and

each R⁴ is a member independently selected from the group consisting of hydrogen, halo,
alkyl, substituted alkyl, acyl, substituted acyl, acylamino, substituted acylamino,
alkylamino, substituted alkylamino, alkylthio, substituted alkylthio, alkoxy,
substituted alkoxy, alkoxycarbonyl, substituted alkoxycarbonyl, alkylarylamino,
substituted alkylarylamino, arylalkyloxy, substituted arylalkyloxy, amino, aryl,
substituted aryl, arylalkyl, substituted arylalkyl, arylsulfonyl, substituted
arylsulfonyl, azido, carboxy, carbamoyl, substituted carbamoyl, carboxyl, cyano,
cycloalkyl, substituted cycloalkyl, cycloheteroalkyl, substituted cycloheteroalkyl,
dialkylamino, substituted dialkylamino, halo, heteroaryloxy, substituted
heteroaryloxy, heteroaryl, substituted heteroaryl, heteroalkyl, substituted
heteroalkyl, hydroxyl, nitro and thio.

35. (Currently amended) A method for treating ~~or preventing cancers, acute lung diseases,~~
~~acute inflammatory exacerbation of chronic lung diseases, surface epithelial cell injury,~~
~~cardiovascular diseases, vasoconstriction, autoimmune disorders or vascular occlusive~~
~~disorders~~ in a subject in need of such treatment, said method comprising administering to
a said subject in need of such treatment or prevention a therapeutically effective amount
of a compound of structural formula Formula (Ia), (II) or (III) wherein said compound of
Formula (Ia) is:



(Ia)

or a pharmaceutically acceptable solvate or hydrate thereof, wherein

n is a member selected from the integers 0 to 5;

R¹ is a member selected from the group consisting of hydrogen, alkyl, substituted

alkyl, acyl, substituted acyl, acylamino, substituted acylamino, alkylamino,

substituted alkylamino, alkylthio, substituted alkylthio, alkoxy, substituted

alkoxy, alkoxycarbonyl, substituted alkoxycarbonyl, alkylarylamino,

substituted alkylarylamino, arylalkyloxy, substituted arylalkyloxy, amino, aryl,

substituted aryl, arylalkyl, substituted arylalkyl, arylamino, substituted

arylamino, arylsulfonyl, substituted arylsulfonyl, carboxy, carbamoyl,

substituted carbamoyl, cycloalkyl, substituted cycloalkyl, cycloheteroalkyl,

substituted cycloheteroalkyl, dialkylamino, substituted dialkylamino,

heteroaryloxy, substituted heteroaryloxy, heteroaryl, substituted heteroaryl,

heteroalkyl, and substituted heteroalkyl;

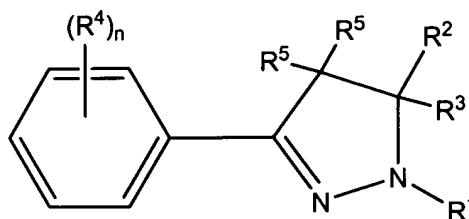
each R², R³ and R⁵ is a member independently selected from the group consisting of

hydrogen, alkyl, substituted alkyl, acyl, substituted acyl, acylamino,

substituted acylamino, alkylamino, substituted alkylamino, alkylthio,

25 substituted alkylthio, alkoxy, substituted alkoxy, alkoxycarbonyl, substituted
26 alkoxycarbonyl, alkylarylamino, substituted alkylarylamino, arylalkyloxy,
27 substituted arylalkyloxy, amino, aryl, substituted aryl, arylalkyl, substituted
28 arylalkyl, arylamino, substituted arylamino, arylsulfonyl, substituted
29 arylsulfonyl, carboxy, carbamoyl, substituted carbamoyl, cycloalkyl,
30 substituted cycloalkyl, cycloheteroalkyl, substituted cycloheteroalkyl,
31 dialkylamino, substituted dialkylamino, heteroaryloxy, substituted
32 heteroaryloxy, heteroaryl, substituted heteroaryl, heteroalkyl, substituted
33 heteroalkyl, hydroxyl, nitro and thio;
34 each R⁴ is a member independently selected from the group consisting of hydrogen, halo,
35 alkyl, substituted alkyl, acyl, substituted acyl, acylamino, substituted acylamino,
36 alkylamino, substituted alkylamino, alkylthio, substituted alkylthio, alkoxy,
37 substituted alkoxy, alkoxycarbonyl, substituted alkoxycarbonyl, alkylarylamino,
38 substituted alkylarylamino, arylalkyloxy, substituted arylalkyloxy, amino, aryl,
39 substituted aryl, arylalkyl, substituted arylalkyl, arylsulfonyl, substituted
40 arylsulfonyl, azido, carboxy, carbamoyl, substituted carbamoyl, carboxyl, cyano,
41 cycloalkyl, substituted cycloalkyl, cycloheteroalkyl, substituted cycloheteroalkyl,
42 dialkylamino, substituted dialkylamino, halo, heteroaryloxy, substituted
43 heteroaryloxy, heteroaryl, substituted heteroaryl, heteroalkyl, substituted
44 heteroalkyl, hydroxyl, nitro and thio;
45 and one or more ~~agonists or~~ antagonists of an Edg receptor.

1 36. (Currently amended) A method for treating ~~or preventing cancers, acute lung diseases,~~
2 ~~acute inflammatory exacerbation of chronic lung diseases, surface epithelial cell injury,~~
3 ~~cardiovascular diseases, vasoconstriction, autoimmune disorders or vascular occlusive~~
4 ~~disorders~~ in a subject in need of such treatment, said method comprising administering to
5 a said subject ~~in need of such treatment or prevention~~ a therapeutically effective amount
6 of a compound of ~~structural formula~~ Formula (Ia), (II) or (III) wherein said compound of
7 Formula (Ia) is:



(Ia)

or a pharmaceutically acceptable solvate or hydrate thereof, wherein

n is a member selected from the integers 0 to 5;

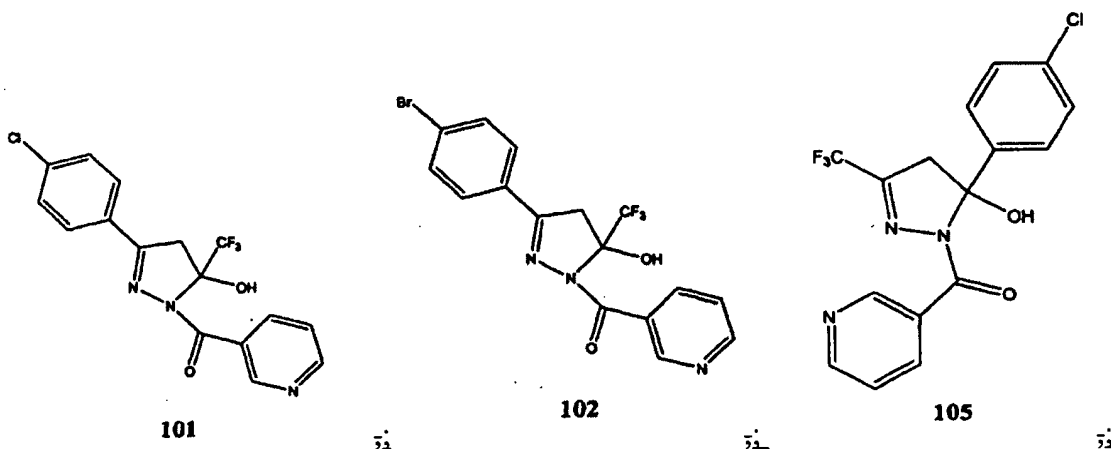
R^1 is a member selected from the group consisting of hydrogen, alkyl, substituted alkyl, acyl, substituted acyl, acylamino, substituted acylamino, alkylamino, substituted alkylamino, alkylthio, substituted alkylthio, alkoxy, substituted alkoxy, alkoxycarbonyl, substituted alkoxycarbonyl, alkylarylamino, substituted alkylarylamino, arylalkyloxy, substituted arylalkyloxy, amino, aryl, substituted aryl, arylalkyl, substituted arylalkyl, arylamino, substituted arylamino, arylsulfonyl, substituted arylsulfonyl, carboxy, carbamoyl, substituted carbamoyl, cycloalkyl, substituted cycloalkyl, cycloheteroalkyl, substituted cycloheteroalkyl, dialkylamino, substituted dialkylamino, heteroaryloxy, substituted heteroaryloxy, heteroaryl, substituted heteroaryl, heteroalkyl, and substituted heteroalkyl;

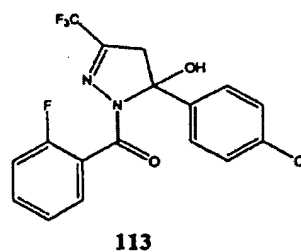
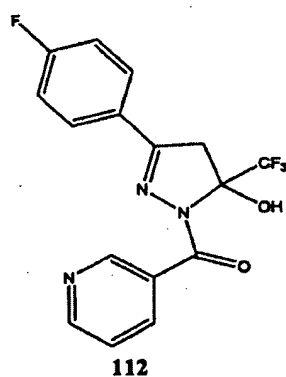
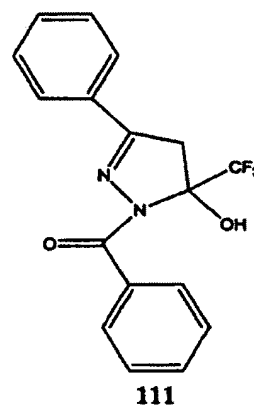
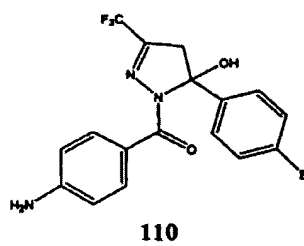
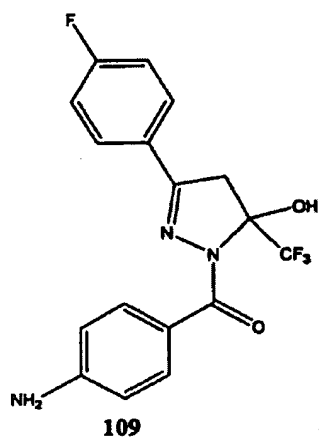
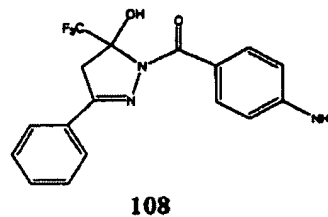
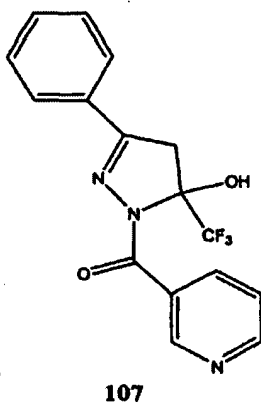
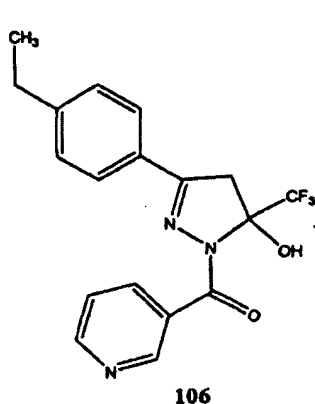
each R^2 , R^3 and R^5 is a member independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, acyl, substituted acyl, acylamino, substituted acylamino, alkylamino, substituted alkylamino, alkylthio, substituted alkylthio, alkoxy, substituted alkoxy, alkoxycarbonyl, substituted alkoxycarbonyl, alkylarylamino, substituted alkylarylamino, arylalkyloxy, substituted arylalkyloxy, amino, aryl, substituted aryl, arylalkyl, substituted arylalkyl, arylamino, substituted arylamino, arylsulfonyl, substituted arylsulfonyl, carboxy, carbamoyl, substituted carbamoyl, cycloalkyl, substituted cycloalkyl, cycloheteroalkyl, substituted cycloheteroalkyl, dialkylamino, substituted dialkylamino, heteroaryloxy, substituted

heteroaryloxy, heteroaryl, substituted heteroaryl, heteroalkyl, substituted heteroalkyl, hydroxyl, nitro and thio;
each R⁴ is a member independently selected from the group consisting of hydrogen, halo, alkyl, substituted alkyl, acyl, substituted acyl, acylamino, substituted acylamino, alkylamino, substituted alkylamino, alkylthio, substituted alkylthio, alkoxy, substituted alkoxy, alkoxycarbonyl, substituted alkoxycarbonyl, alkylarylamino, substituted alkylarylamino, arylalkyloxy, substituted arylalkyloxy, amino, aryl, substituted aryl, arylalkyl, substituted arylalkyl, arylsulfonyl, substituted arylsulfonyl, azido, carboxy, carbamoyl, substituted carbamoyl, carboxyl, cyano, cycloalkyl, substituted cycloalkyl, cycloheteroalkyl, substituted cycloheteroalkyl, dialkylamino, substituted dialkylamino, halo, heteroaryloxy, substituted heteroaryloxy, heteroaryl, substituted heteroaryl, heteroalkyl, substituted heteroalkyl, hydroxyl, nitro and thio;

and one or more drugs useful in treating ~~or preventing cancers, acute lung diseases, acute inflammatory exacerbation of chronic lung diseases, surface epithelial cell injury, cardiovascular diseases, vasoconstriction[[,]] autoimmune disorders or vascular occlusive disorders.~~

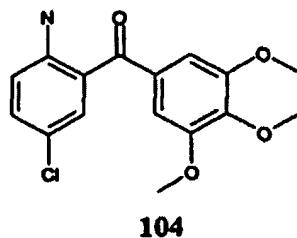
37. (Currently amended) The method of Claim ~~[[28]]~~ 1 or 2, wherein the modulator is a compound of a formula that is selected from the ~~group consisting of:~~





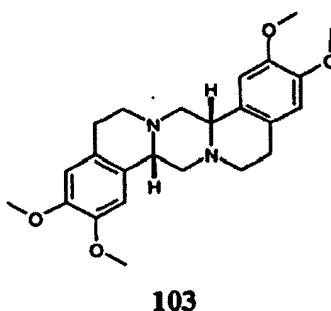
and

38. (Withdrawn) The method of Claim 29, wherein the modulator is a compound of formula



2

- 1 **39.** (Withdrawn) The method of Claim 30, wherein the modulator is a compound of formula



2

- 1 **40.** (Withdrawn) The method of Claim 1 or 2, wherein the biological activity is an immune
2 response.

- 1 **41.** (Withdrawn) The method of Claim 40, wherein the immune response is stimulated by
2 SIP.

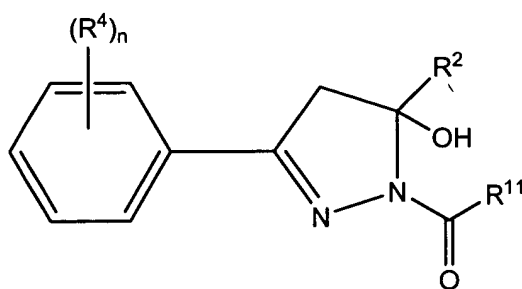
- 1 **42.** (Withdrawn, Currently amended) A method for treating ~~or preventing~~ a disorder in a
2 subject, comprising administering to a said subject in need of such treatment ~~or~~
3 ~~prevention~~ a therapeutically effective amount of a compound of ~~structural formula~~
4 Formulae (I), (II) or (III), wherein the compound of ~~structural formula~~ Formulae (I), (II)
5 or (III) stimulates the immune system.

- 1 **43.** (Withdrawn) The method of Claim 42, wherein the subject suffers from an inherited
2 immune deficiency.

- 1 44. (Withdrawn, Currently amended) The method of Claim 42, wherein the compound of
2 ~~structural formula~~ Formulae (I), (II) or (III) is administered as an adjuvant to a vaccine.
- 1 45. (Withdrawn) The method of Claim 42, wherein the subject is infected with a virus.
- 1 46. (Withdrawn) The method of Claim 45, wherein the virus is selected from the group
2 consisting of cytomegalovirus, herpes simplex virus I, herpes simplex virus II, influenza
3 A virus, influenza B virus, hepatitis A virus, hepatitis C virus, hepatitis C virus, and
4 human immunodeficiency virus.
- 1 47. (Withdrawn, Currently amended) A method for treating ~~or preventing~~ an immune
2 disorder in a subject, comprising administering to a said subject in need of such treatment
3 ~~or prevention~~ a therapeutically effective amount of a compound of ~~structural formula~~
4 Formulae (I), (II) or (III), wherein the immune disorder is characterized by inappropriate
5 activation of the immune system.
- 1 48. (Withdrawn, Currently amended) The method of Claim 47, wherein the compound of
2 ~~structural formula~~ Formulae (I), (II) or (III) suppresses the immune system of the subject.
- 1 49. (Withdrawn) The method of Claim 48, wherein the subject is afflicted with a disorder
2 that is selected from the group consisting of systemic lupus erythematosus, rheumatic
3 cardiatis, polymyositis, pemphigus, bullous dermatitis herpetiformis, Stevens-Johnson
4 syndrome, mycosis fungoides, dermatitis, ulcerative colitis, Crohn's disease, intractable
5 sprue, idiopathic thrombocytopenic purpura, hemolytic anemia, erythroblastopenia,
6 congenital hypoplastic anemia, osteoarthritis, rheumatoid arthritis, bursitis, acute gouty
7 arthritis, epicondylitis, acute nonspecific tenosynovitis, multiple sclerosis, keratitis,
8 iritis, iridocyclitis, chorioretinitis, choroiditis, optic neuritis, sarcoiodosis, Loeffler's
9 syndrome, berylliosis, tuberculosis, spondylitis, tenosynovitis, psoriatic arthritis, and type I
10 diabetes mellitus.

50. (Withdrawn) The method of Claim 48, wherein the subject is the recipient of a transplanted cell, tissue, or organ.

51. (New) A method of treating vasoconstriction in a patient comprising:
administering to the patient a therapeutically effective amount of a modulator of an Edg-1 receptor wherein the modulator is a compound of Formula (Ib) is:



(Ib)

or a pharmaceutically acceptable solvate or hydrate thereof, wherein

n is a member selected from the integers 0 to 5;

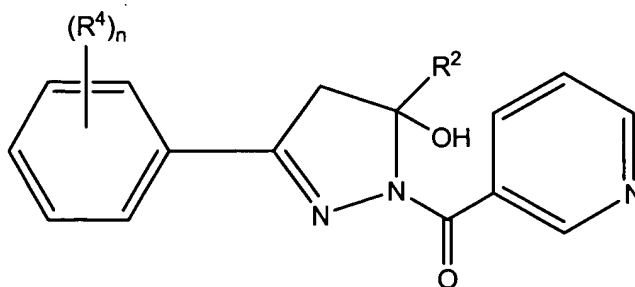
R^{11} is an aryl group;

each R^2 and R^4 is a member independently selected from the group consisting of

hydrogen, halo, alkyl, substituted alkyl, acyl, substituted acyl, acylamino, substituted acylamino, alkylamino, substituted alkylamino, alkylthio, substituted alkylthio, alkoxy, substituted alkoxy, alkoxycarbonyl, substituted alkoxycarbonyl, alkylarylamino, substituted alkylarylamino, arylalkyloxy, substituted arylalkyloxy, amino, aryl, substituted aryl, arylalkyl, substituted arylalkyl, arylamino, substituted arylamino, arylsulfonyl, substituted arylsulfonyl, carboxy, carbamoyl, substituted carbamoyl, cycloalkyl, substituted cycloalkyl, cycloheteroalkyl, substituted cycloheteroalkyl, dialkylamino, substituted dialkylamino, heteroaryloxy, substituted heteroaryloxy, heteroaryl, substituted heteroaryl, heteroalkyl, substituted heteroalkyl, hydroxyl, nitro and thio.

1 **52.** (New) The method of claim 51, wherein said aryl group in R^{11} is a heteroaryl group.

1 **53.** (New) The method of claim 52, wherein said compound has the formula:



1 **54.** (New) The method of claim 53, wherein R^2 is a substituted alkyl group.

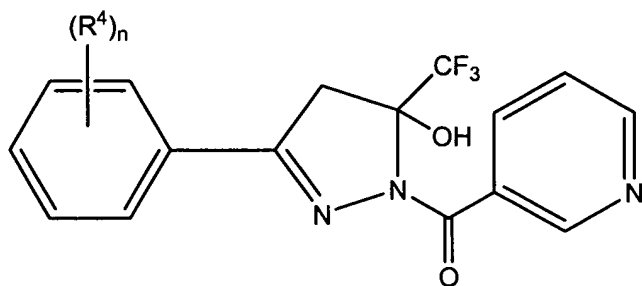
1 **55.** (New) The method of claim 54, wherein R^2 is said substituted alkyl group is $-CF_3$.

1 **56.** (New) The method of claim 55, wherein n is 1.

1 **57.** (New) The method of claim 56, wherein R^4 is a halo group.

1 **58.** (New) The method of claim 57, wherein said halo group is chlorine.

2 **59.** (New) A method of treating vasoconstriction in a patient comprising:
3 administering to the patient a therapeutically effective amount of a modulator of an Edg-1
4 receptor wherein the modulator is a compound of Formula (Ic):



(Ic)

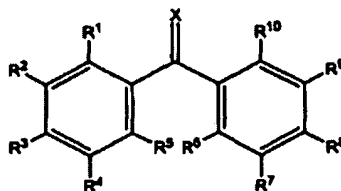
n is a member selected from the integers 0 to 5;
each R⁴ is a member independently selected from the group consisting of hydrogen, halo, alkyl, substituted alkyl, acyl, substituted acyl, acylamino, substituted acylamino, alkylamino, substituted alkylamino, alkylthio, substituted alkylthio, alkoxy, substituted alkoxy, alkoxycarbonyl, substituted alkoxycarbonyl, alkylaryl amino, substituted alkylaryl amino, arylalkyloxy, substituted arylalkyloxy, amino, aryl, substituted aryl, arylalkyl, substituted arylalkyl, arylamino, substituted arylamino, arylsulfonyl, substituted arylsulfonyl, carboxy, carbamoyl, substituted carbamoyl, cycloalkyl, substituted cycloalkyl, cycloheteroalkyl, substituted cycloheteroalkyl, dialkylamino, substituted dialkylamino, heteroaryloxy, substituted heteroaryloxy, heteroaryl, substituted heteroaryl, heteroalkyl, substituted heteroalkyl, hydroxyl, nitro and thio.

60. (New) The method of claim 59, wherein n is 1.

61. (New) The method of claim 60, wherein R⁴ is a halo group.

62. (New) The method of claim 61, wherein said halo group is chlorine.

63. (New) A method of modulating an Edg-1 receptor mediated biological activity in a subject, comprising administering to the subject a therapeutically effective amount of a non-phospholipid modulator of the Edg-1 receptor, wherein the modulator is a compound of Formula (II):



(II)

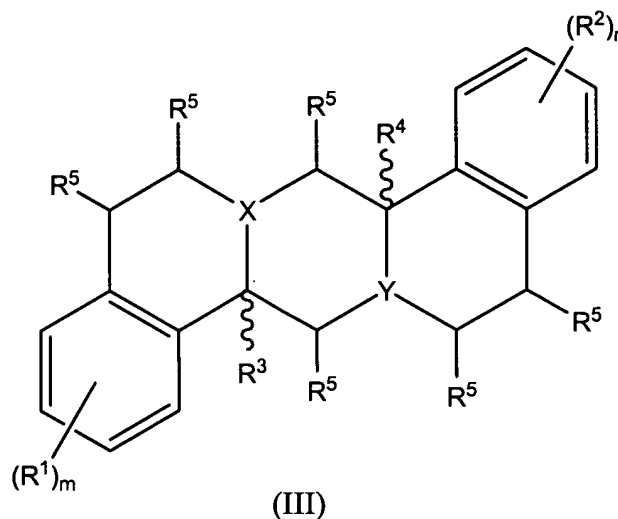
or a pharmaceutically acceptable solvate or hydrate thereof, wherein

X is a member selected from the group consisting of O and S;

each R¹, R², R³, R⁴ and R⁵ is a member independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, acyl, substituted acyl, acylamino, substituted acylamino, alkylamino, substituted alkylamino, alkylthio, substituted alkylthio, alkoxy, substituted alkoxy, alkoxycarbonyl, substituted alkoxycarbonyl, alkylarylamino, substituted alkylarylamino, arylalkyloxy, substituted arylalkyloxy, amino, aryl, substituted aryl, arylalkyl, substituted arylalkyl, arylsulfonyl, substituted arylsulfonyl, azido, carboxy, carbamoyl, substituted carbamoyl, carboxyl, cyano, cycloalkyl, substituted cycloalkyl, cycloheteroalkyl, substituted cycloheteroalkyl, dialkylamino, substituted dialkylamino, halo, heteroaryloxy, substituted heteroaryloxy, heteroaryl, substituted heteroaryl, heteroalkyl, substituted heteroalkyl, hydroxyl, nitro and thio; and

each R⁶, R⁷, R⁸, R⁹ and R¹⁰ is a member independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, acyl, substituted acyl, acylamino, substituted acylamino, alkylamino, substituted alkylamino, alkylthio, substituted alkylthio, alkoxy, substituted alkoxy, alkoxycarbonyl, substituted alkoxycarbonyl, alkylarylamino, substituted alkylarylamino, arylalkyloxy, substituted arylalkyloxy, amino, aryl, substituted aryl, arylalkyl, substituted arylalkyl, arylsulfonyl, substituted arylsulfonyl, azido, carboxy, carbamoyl, substituted carbamoyl, carboxyl, cyano, cycloalkyl, substituted cycloalkyl, cycloheteroalkyl, substituted cycloheteroalkyl, dialkylamino, substituted dialkylamino, halo, heteroaryloxy, substituted heteroaryloxy, heteroaryl, substituted heteroaryl, heteroalkyl, substituted heteroalkyl, hydroxyl, nitro and thio.

64. (New) A method of modulating an Edg-1 receptor mediated biological activity in a subject, comprising administering to the subject a therapeutically effective amount of a non-phospholipid modulator of the Edg-1 receptor, wherein the modulator is a compound of Formula (III):



or a pharmaceutically acceptable solvate or hydrate thereof, wherein

n is a member selected from the integers 1 to 4;

m is a member selected from the integers 1 to 4;

each X and Y is a member independently selected from the group consisting of C and N; and

each R¹, R², R³, R⁴ and R⁵ is a member independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, acyl, substituted acyl, acylamino, substituted acylamino, alkylamino, substituted alkylamino, alkylthio, substituted alkylthio, alkoxy, substituted alkoxy, alkoxycarbonyl, substituted alkoxycarbonyl, alkylaryl amino, substituted alkylaryl amino, arylalkyloxy, substituted arylalkyloxy, amino, aryl, substituted aryl, arylalkyl, substituted arylalkyl, arylsulfonyl, substituted arylsulfonyl, azido, carboxy, carbamoyl, substituted carbamoyl, carboxyl, cyano, cycloalkyl, substituted cycloalkyl, cycloheteroalkyl, substituted cycloheteroalkyl, dialkylamino, substituted dialkylamino, halo, heteroaryloxy, substituted heteroaryloxy, heteroaryl, substituted heteroaryl, heteroalkyl, substituted heteroalkyl, hydroxyl, nitro and thio.